

**REMARKS**

Applicant respectfully requests favorable reconsideration of this application, as amended.

Claims 70, 72–79 and 92–104 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, Claims 70 and 98 were rejected as reciting “a tissue sample” on the first, fifth and sixth lines of each claim.<sup>1</sup> In response, Claims 70 and 98 have been amended to recite a single instance of the term “a tissue sample.” Applicant respectfully submits that the § 112 rejections have been overcome.

Claims 70, 72–79, 96–104 were finally rejected under 35 U.S.C. § 102(b) as being anticipated by Northrup (US 5639423), while Claims 92–96 were finally rejected under 35 U.S.C. § 103(a) as being unpatentable over Northrup in view of Chu (US 5,958,341). Without acceding to the rejections under § 102, Claims 70 and 98 have been amended to recite several features of the claimed invention more clearly. Additionally, Claims 72–75 and 100–103 have been amended to comport with the recitation of “at least one sensor” within Claims 70 and 98, respectively, and Claims 77–79, 92–95 and 99 have been amended for reasons unrelated to patentability. No new matter has been added. Applicant respectfully submits that none of the references of record teaches or suggests all of the features recited by the claims.

Northrup discloses an integrated microfabricated instrument for the manipulation, reaction and detection of microliter to picoliter samples for DNA-based reactions, such as the polymerase chain reaction (or PCR). Northrup teaches that the small size of his reaction chamber facilitates rapid thermal cycling, and that Lamb-wave devices may be used as sensors, pumps and agitators. See, e.g., Abstract; Col. 3:39–49; Col. 4:49–65; Col. 7:29–31, 35–41, 61–62; Col. 8:20–23; etc. Northrup generally teaches that ultrasonic waves are used to manipulate cells and cell-contents “by stirring and or mixing reagents from other chambers on the microinstrument” (Col. 5:42–52). During the PCR reaction, Northrup specifically discloses that his Lamb-wave transducer,  $LW_C$ , is used as an “agitator or mixer as described below to mix the reagents and promote the reaction” within reaction chamber 30 (Col. 8:21–23). Thus, Northrup teaches that his Lamb-wave transducer  $LW_C$  agitates or mixes the contents of reaction chamber 30 during a particular reaction.

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<sup>1</sup> See, Office Action at Page 2 (Paragraphs 4–7).

Northrup fails to teach or suggest a reaction chamber that includes a solution for fixing a tissue sample placed therein with no or minimal damage, as recited by Claims 70 and 98. Instead, as noted above, Northrup's Lamb-wave transducer LW<sub>c</sub> merely agitates or mixes the contents of reaction chamber 30. *See*, also, Col. 7:29–34 ("The Lamb-wave transducer LW<sub>c</sub> acts as an agitator, mixer"); Col. 11:31–38 ("By sending Lamb-waves from left to right ... and Lamb-waves from right to left ... a stirring or circulating action is produced"). Furthermore, Northrup teaches away from fixing a tissue sample in his reaction chamber because he also discloses that sonication may be used to disrupt and expose cell components through lysis, which are then used by subsequent processes. *See*, e.g., Col. 5:44–47, 52–57, 57–61. Thus, Northrup also teaches that this pre-PCR use of ultrasound leads to the destruction of his samples rather than their preservation.<sup>2</sup> Consequently, Northrup fails to teach or suggest that a tissue sample may be fixed in a solution within a reaction chamber with no or minimal damage, as recited by Claims 70 and 98.<sup>3</sup>

Northrup also fails to teach or suggest a central processing unit, coupled to the ultrasound generator and the sensor, to control the ultrasound generator by adjusting at least one of a frequency and an intensity of the ultrasound energy, in response to a signal received from the sensor, to fix the tissue sample in the solution with no or minimal damage, as recited by Claims 70 and 98. The Office Action alleges that these features merely represent an "intended use" of the central processing unit, and, as such, provide no patentable weight to these claims because "the prior art structure is capable of performing the intended use" (Office Action at Page 4). Applicant disagrees.

Northrup fails to disclose a central processing unit that is coupled to his Lamb-wave transducer LW<sub>c</sub> and his Lamb-wave sensor LW<sub>b</sub>. While Northrup does disclose, generally, the concept that "detection signals may be processed and stored by integrated microelectronic devices so that result interpretation and control mechanisms (which may utilize feedback) can

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<sup>2</sup> The instant application seeks to preserve the morphology of samples, for subsequent processes, in order to provide information about proteins and nucleic acids, as well as the histological appearance of the tissue sample. Indeed, Northrup's "subsequent techniques," discussed, for example, at Col. 6:1-10, do not involve any quality of the sample other than the extracted DNA.

<sup>3</sup> The Office Action also opines that, with respect Northrup's "PCR and subsequent techniques (column 5, lines 42-61) ... the solutions (reagents) used in the chamber (column 7, lines 29-35) disclosed by Northrup et al. would be for processing or fixing" (Page 3, Paragraph 9). While Applicant agrees that the reagent within Northrup's reaction chamber 30 is used "for processing," there is simply no teaching or suggestion that this reagent is used "for fixing" the sample.

be integrally contained on the microinstrument" (Col. 4:41–44), Northrup simply fails to suggest that a central processing unit may be used within his system. To the contrary, Northrup teaches that his Lamb-wave device includes various inductors ( $L_{xy}$ ), capacitors ( $C_{xy}$ ) and transducers ( $LW_i$ ) that are excited at a specific frequency that corresponds to the resonant frequency of these electrical and mechanical components. Moreover, Northrup fails to disclose a feedback or control loop for his Lamb-wave device, i.e., only a single, resonant operating mode is disclosed, and no suggestion of adjusting the frequency or intensity of the ultrasound energy in response to a signal from his Lamb-wave sensor  $LW_D$  is provided. See, generally, Col. 7:42 to Col. 8:8; Col. 7:47–49 ("Lamb-wave transducers have high mechanical Q values and can therefore be powered by only a narrow range of alternating voltage frequencies"). Consequently, Northrup fails to teach or suggest a central processing unit, coupled to the ultrasound generator and the sensor, to control the ultrasound generator by adjusting at least one of a frequency and an intensity of the ultrasound energy, in response to a signal received from the sensor, to fix the tissue sample in the solution with no or minimal damage, as recited by Claims 70 and 98.

Additionally, Northrup fails to disclose a transducer that generates ultrasound of a frequency of at least 100 KHz, as recited by Claim 98 (as well as dependent Claim 77). Instead, Northrup's Lamb-waves "have frequencies in the approximate range of 1 to 200 MHz" (Col. 11:4–6). Consequently, Northrup fails to teach or suggest this feature.

Moreover, none of the remaining references of record cure Northrup's deficiencies.

Accordingly, Claims 70 and 98 are allowable over the cited references. Claims 70, 72–79 and 92–96, depending from Claim 70, and Claims 99–104, depending from Claim 98, are also allowable, at least for the reasons discussed above.

In view of the amendments and remarks presented herein, Applicant respectfully submits that this application is in condition for allowance and should now be passed to issue.

A Notice of Allowance is respectfully solicited.

If any extension of time is required in connection with the filing of this paper and has not been requested separately, such extension is hereby requested.

The Commissioner is hereby authorized to charge any fees and to credit any overpayments that may be required by this paper under 37 C.F.R. §§ 1.16 and 1.17 to Deposit Account No. 02-2135.

Respectfully submitted,

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